ISSN 1070-4280, Russian Journal of Organic Chemistry, 2007, Vol. 43, No. 2, pp. 224–227. © Pleiades Publishing, Ltd. 2007.
Original Russian Text © E.S. Vostrov, A.A. Novikov, A.N. Maslivets, Z.G. Aliev, 2007, published in Zhurnal Organicheskoi Khimii, 2007, Vol. 43, No. 2, pp. 232–235.

Cyclization of Aroylacetic Acids 2-Carboxyphenylamides into 2-[(*Z*)-2-Aryl-2-hydroxy-1-ethenyl]-4*H*-3,1-benzoxazin-4-ones. Crystal and Molecular Structure of 2-[(*Z*)-2-Hydroxy-2-phenyl-1-ethenyl]-4*H*-3,1-benzoxazin-4-one

E. S. Vostrov[a], A. A. Novikov[a], A. N. Maslivets[a], and Z. G. Aliev[b]

[a]*Perm State University, Perm 614990 Russia*
e-mail: koh2@psu.ru
[b]*Institute of Problems of Chemical Physics, Russian Academy of Sciences, Chernogolovka*

Received April 5, 2006

Abstract—2-Carboxyphenylamides of aroylacetic acids undergo cyclization when treated with dehydrating agents to give 2-[(*Z*)-2-aryl-2-hydroxy-1-ethenyl]-4*H*-3,1-benzoxazin-4-ones. Crystal and molecular structure of the latter phenyl derivative was studied by X-ray crystallography.

DOI: 10.1134/S1070428007020121

Heterocyclic enaminoketones, namely, 3-acylmethylene-3,4-dihydro-2*H*-1,4-benzoxazin-2-ones [1], 3-acylmethylene-1,2,3,4-tetrahydroquinoxalin-2-ones [2], 3-acylmethylene-3,4-dihydro-2-phenylquinoxalines [3], 2-acylmethylene-3-aryl-1,2,3,4-tetrahydro-4-quinazolones [4], and 3-acylmethylenepiperazin-2-ones [5], exist in enaminoketone form as demonstrated by X-ray diffraction studies. In all compounds investigated an intramolecular hydrogen bond of H-chelate type was observed between the NH group of the heterocycle and the carbonyl of acylmethylene fragment; therewith the hydrogen involved into the hydrogen bond was localized at the nitrogen of the enaminoketone moiety.

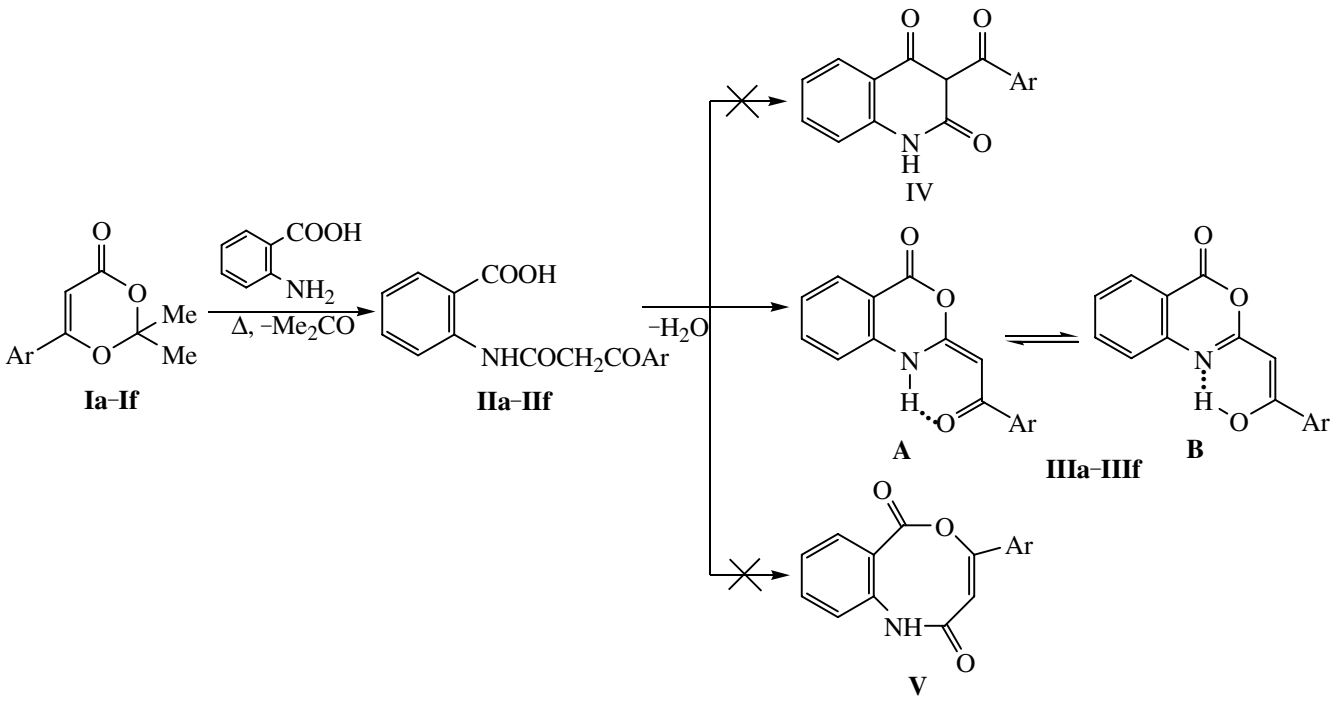
In extension of studies on the synthesis of new classes of heterocyclic enaminoketones and on investigating fine features of their structure we performed intramolecular cyclization of aroylacetic acids 2-carboxyanilides by treating them with dehydrating agents. The arising benzoxazinones are polyfunctional reagents and can serve as starting compounds for the synthesis of representatives of new classes of extensively studied nowadays dioxoheterocycles and heterocumulenes based thereon.

Two convenient methods were published for preparation of aroylacetamides: aroylacylation of amines [6] and amides [7] with aroylketenes generated by thermolysis of 6-aryl-2,2-dimethyl-4*H*-1,3-dioxin-4-ones, and reaction of ethyl benzoylacetate with arylamines [8]. We used the former procedure for preparation of aroylacetic acids 2-carboxyphenylamides, initial compounds for investigation of intramolecular cyclization.

Boiling at 137–138°C for 15–20 min of solutions in *m*-xylene of 6-aryl-2,2-dimethyl-4*H*-1,3-dioxin-4-ones **Ia–If** in the presence of an equivalent amount of anthranilic acid led to the formation of aroylacetic acids 2-carboxyphenylamides **IIa–IIf**. Spectral characteristics of anilides **IIa–IIf** are reported in EXPERIMENTAL and are well consistent with those of similar in structure aroylacetic acids amides [6–8].

Anilides **IIa–IIf** taken in the ratio 1:1 with dehydrating agents, e.g., at boiling in benzene with acetic anhydride for 1.5–2 h (method *a*) or at boiling in dichloroethane with dicyclohexylcarbodiimide for 25–30 min (method *b*) yielded light-yellow crystalline compounds **IIIa–IIIf**. For the obtained products of the intramolecular cyclization of anilides **IIa–IIf** we failed to make unambiguous choice among isomeric structures: based only on spectral data 2-aroylmethylene-1,2-dihydro-4*H*-3,1-benzoxazin-4-ones (**A**, **B**), 3-aroyl-1,2,3,4-tetrahydroquinolin-2,4-diones **IV**, or 4-aryl-1,6-dihydro-2*H*-benzo[*C*][1,5]oxazocine-2,6-diones **V**, and also to establish the localization in the compounds of the hydrogen involved into the intramolecular hydrogen bond. Therefore the application of X-ray crystallography was necessary. The X-ray diffraction analysis showed that compound **IIIa** was 2-[(*Z*)-2-hydroxy-2-phenyl-1-ethenyl]-4*H*-3,1-benzoxazin-4-one.

Scheme.



Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-$EtOC_6H_4$ (**d**), 4-ClC_6H_4 (**e**), 4-BrC_6H_4 (**f**).

A single crystal of compound **IIIa** was specially grown from benzene for the X-ray diffraction study. The general view of **IIIa** molecule is presented on the figure.

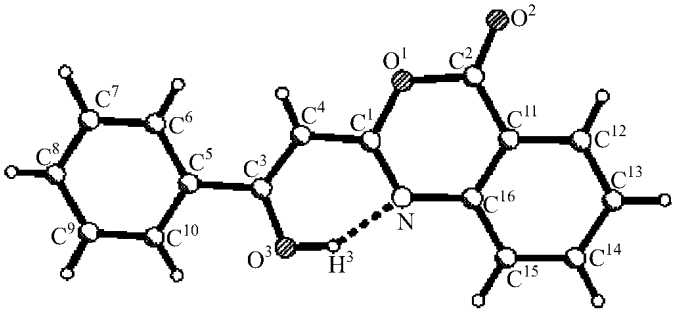
The main bond lengths in the molecule are given below. The analysis of these interatomic distances unambiguously shows that the hydrogen atom is localized on the oxygen. The molecule is virtually planar containing an intramolecular hydrogen bond O–H···N. The distance $N\cdots H^3$ equals 1.71 Å, and the angle at the hydrogen is 146°.

Bond	*d*, Å
O^1–C^1	1.368(3)
O^1–C^2	1.393(3)
O^2–C^2	1.199(3)
O^3–C^3	1.311(3)
N–C^1	1.305(3)
C^1–C^4	1.411(4)
C^3–C^4	1.366(4)
C^3–C^5	1.486(4)

Thus the intramolecular cyclization of anilides **II** effected by dehydrating agents resulted in formation of benzoxazinones **IV**. At the same time the localization of hydrogen in the enaminoketone fragment at the oxygen atom of the hydroxyenimine fragment tautomeric to the enaminoketone one is not only quite unexpected, but obviously contrasts with the structure of the formerly studied heterocyclic enaminoketones [1–5]; the reason of this phenomenon requires a separate study. It should also be noted that the established localization of the hydrogen suggests new interpretation of the abnormal results of reactions between some heterocyclic enaminoketones with oxalyl chloride leading to the closure of a furandione [9, 10] and not a pyrroledione ring.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer UR-20 from mulls in mineral oil. ^1H and ^{13}C NMR spectra were registered on a spectrometer Bruker AM-400 (400 MHz), internal reference TMS. Mass spectra were taken



Structure of 2-[(*Z*)-2-hydroxy-2-phenyl-1-ethenyl]-4*H*-3,1-benzoxazin-4-one (**IIIa**).

on MKh-1320, ionizing electrons energy 70eV. The homogeneity of compounds synthesized was confirmed by TLC on Silufol plates, eluent benzene–ethyl acetate, 5:1, development in iodine vapor.

Benzoylacetic acid *N*-(2-carboxyphenyl)amide (IIa). A solution of 4.9 mmol of dioxinone **Ia** and 4.9 mmol of anthranilic acid in 2 ml of *m*-xylene was boiled for 10–15 min, cooled, the precipitate was filtered off. Yield 1.10 g (79%), mp 177–178°C (ethanol). IR spectrum, ν, cm^{-1}: 3160 br (NH, COOH), 1698 (COOH), 1685 br (CONH, COPh), 1540 ("amide II"). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 4.31 s (2H, CH_2), 7.18–8.44 group of signals (9H, C_6H_4 + Ph), 11.26 s (1H, NH), 13.60 br.s (1H, COOH). Found, %: C 67.76; H 4.60; N 5.00. $C_{16}H_{13}NO_4$. Calculated, %: C 67.84; H 4.63; N 4.94.

Compounds **IIb–IIf** were similarly obtained.

4-Toluoylacetic acid N-(2-carboxyphenyl)amide (IIb). Yield 1.12 g (77%), mp 157–158°C (ethanol). IR spectrum, ν, cm^{-1}: 3150 br (NH, COOH), 1700 (COOH), 1675 br (CONH, COC_6H_4), 1535 ("amide II"). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.40 s (3H, Mε), 4.16 s (2H, CH_2), 7.11–8.69 group of signals (8H, $2C_6H_4$), 11.38 s (1H, NH). Found, %: C 68.70; H 5.08; N 4.73. $C_{17}H_{15}NO_4$. Calculated, %: C 68.68; H 5.09; N 4.71.

4-Methoxybenzoylacetic acid *N*-(2-carboxyphenyl)amide (IIc). Yield 1.07 g (70%), mp 175–176°C (ethanol). IR spectrum, ν, cm^{-1}: 3145 br (NH, COOH), 1703 (COOH), 1670 br (CONH, COC_6H_4), 1533 ("amide II"). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.86 s (3H, MeO), 4.22 s (2H, CH_2), 7.05–8.44 group of signals (8H, $2C_6H_4$), 11.26 C (1H, NH), 13.58 br.s (1H, COOH). Found, %: C 65.25; H 4.80; N 4.45. $C_{17}H_{15}NO_5$. Calculated, %: C 65.17; H 4.83; N 4.47.

4-Ethoxybenzoylacetic acid *N*-(2-carboxyphenyl)amide (IId). Yield 1.11 g (69%), mp 192–193°C (ethanol). IR spectrum, ν, cm^{-1}: 3145 br (NH, COOH), 1680 (COOH), 1660 br (CONH, COC_6H_4), 1533 ("amide II"). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.44 t (3H, $\underline{Me}CH_2O$, *J* 7.0 Hz), 4.10 q (2H, $MeCH_2O$, *J* 7.0 Hz), 4.10 s (2H, CH_2), 6.91–8.71 group of signals (8H, $2C_6H_4$), 11.41 s (1H, NH). Found, %: C 66.04; H 5.24; N 4.30. $C_{18}H_{17}NO_5$. Calculated, %: C 66.05; H 5.23; N 4.28.

4-Chlorobenzoylacetic acid *N*-(2-carboxyphenyl)amide (IIe). Yield 1.18 g (76%), mp 170–171°C (ethanol). IR spectrum, ν, cm^{-1}: 3225 br (NH, COOH), 1718 (COOH), 1685 br (CONH, COC_6H_4), 1536 («amide II»). ^1H (DMSO-d_6), δ, ppm: 4.31 s (2H, CH_2), 7.18–8.40 group of signals (8H, $2C_6H_4$), 11.23 s (1H, NH), 13.58 br.s (1H, COOH). Found, %: C 60.50; H 3.80; Cl 11.20; N 4.42. $C_{16}H_{12}ClNO_4$. Calculated, %: C 60.48; H 3.81; Cl 11.16; N 4.41.

4-Bromobenzoylacetic acid *N*-(2-carboxyphenyl)amide (IIf). Yield 1.38 g (78%), mp 190–191°C (ethanol). IR spectrum, ν, cm^{-1}: 3335 br (NH, COOH), 1698 (COOH), 1680 br (CONH, COC_6H_4), 1533 ("amide II"). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 4.12 s (2H, CH_2), 7.13–8.76 group of signals (8H, $2C_6H_4$), 11.38 s (1H, NH). Found, %: C 53.04; H 3.35; Br 22.10; N 3.85. $C_{16}H_{12}BrNO_4$. Calculated, %: C 53.06; H 3.34; Br 22.06; N 3.87.

2-[(*Z*)-2-Hydroxy-2-phenyl-1-ethenyl]-4*H*-3,1-benzoxazin-4-one (IIIa). *a*. A solution of 3.35 mmol of anilide **IIa** and 3.35 mmol of acetic anhydride in 10 ml of benzene was boiled for 2 h, evaporated, and the residue was crystallized from 2-propanol. Yield 0.89 g(100%).

b. A solution of 3.35 mmol of anilide **IIa** and 3.35 mmol of dicyclohexylcarbodiimide in 20 ml of 1,2-dichloroethane was boiled for 39 min, cooled, the precipitate of dicyclohexylurea was filtered off, the filtrate was evaporated, and the residue was crystallized from 2-propanol. Yield 0.89 g (100%), mp 141–142°C (2-propanol). IR spectrum, ν, cm^{-1}: 3050 br (OH_{bound}), 1762 (C^4=O), 1634 (C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 5.96 s (1H, CH), 7.37–8.15 group of signals (9H, Ph + C_6H_4), 14.26 s (1H, OH). Found, %: C 72.39; H 4.15; N 5.30. $C_{16}H_{11}NO_3$. Calculated, %: C 72.45; H 4.18; N 5.28.

X-ray crystallography. Crystals of compound **IIIa**, $C_{16}H_{11}NO_3$, monoclinic, *a* 14.182(3), *b* 9.443(2), *c* 9.404 (2) Å, β 97.86(3)°, *V* 1247.6(5) $Å^3$, *M* 265.26, d_{calc} 1.412 g/cm^3, *Z* 4, space group $P2_1/n$. The set of experimental reflections was obtained on an automatic four-circle diffractometer QM-4 (KUMA DIFFRACTION) with κ-geometry by ω/2Θ scanning on MoK_α-radiation with a monochromator ($2\Theta \le 50.1°$). Overall 2349 reflections were measured, 2206 among them independent (R_{int} 0.0495). The correction for extinction was not done (μ 0.10 mm^{-1}). The structure was solved by the direct method by the program SIR92 [11] followed by calculation of a series of electron density charts. Hydrogen atoms were revealed from the difference synthesis of the electron density. Full-matrix refining in anisotropic approximation for nonhydrogen atoms was performed by the least-mean-squares method using SHELXL-97 software[12] and was completed at R_1 0.0393, wR_2 0.1070 using 1027 reflections with $I \ge 2\sigma(I)$ and R_1 0.1340, wR_2 0.1744 using all 2206 reflections.

Analogously were prepared compounds **IIIb–IIIf**.

2-[(*Z*)-2-Hydroxy-2-(4-methylphenyl)-1-ethenyl]-4*H*-3,1-benzoxazin-4-one (IIIb). Yield 98 (*a*), 100% (*α*), mp 178–179°C (2-propanol). IR spectrum, ν, cm^{-1}: 3080 br (OH_{bound}), 1770 (C^4=O), 1640 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.42 s (3H, Me), 5.93 s (1H, CH), 7.26–8.14 group of signals (8H, $2C_6H_4$), 14.25 s (1H, OH). Found, %: C 73.10; H 4.67; N 5.03. $C_{17}H_{13}NO_3$. Calculated, %: C 73.11; H 4.69; N 5.01.

2-[(*Z*)-2-Hydroxy-2-(4-methoxyphenyl)-1-ethenyl]-4*H*-3,1-benzoxazin-4-one (IIIc). Yield 100% (*a*, *b*), mp 164–165°C (2-propanol). IR spectrum, ν, cm^{-1}: 3040 br (OH_{bound}), 1750 (C^4=O), 1615 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.88 s (3H, MeO), 5.88 s (1H, CH), 6.96–8.13 group of signals (8H, $2C_6H_4$), 14.27 s (1H, OH). ^{13}C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 55.48 (MeO), 83.93 (C^2=<u>C</u>H), 114.10 (C^{4a}), 121.25–129.35 (ArH), 137.00 (C^{8a}), 162.12 (C^4), 162.56 (C^2), 177.30 (<u>C</u>OC_6H_4). Mass spectrum, *m/z* (I_{rel}, %): 265 (32) $[M]^+$, 188 (6) $[M - C_6H_5]^+$, 146 (3) $[M - C_6H_5COCH_2]^+$, 119 (19) $[C_6H_5COCH_2]^+$, 105 (100) $[C_6H_5CO]^+$, 77 (29) $[C_6H_5]^+$. Found, %: C 69.17; H 4.48; N 4.75. $C_{17}H_{13}NO_4$. Calculated, %: C 69.15; H 4.44; N 4.74.

2-[(*Z*)-2-Hydroxy-2-(4-ethoxyphenyl)-1-ethenyl]-4*H*-3,1-benzoxazin-4-one (IIId). Yield 98 (*a*), 100% (*b*), mp 165–166°C (2-propanol). IR spectrum, ν, cm^{-1}: 3040 br (OH_{bound}), 1753 (C^4=O), 1630 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.45 t (3H, <u>Me</u>CH_2O, *J* 7.0 Hz), 4.88 q (2H, MeCH_2O, *J* 7.0 Hz), 5.88 s (1H, CH), 6.94–8.12 group of signals (8H, $2C_6H_4$), 14.27 s (1H, OH). Found, %: C 69.90; H 4.88; N 4.55. $C_{18}H_{15}NO_4$. Calculated, %: C 69.89; H 4.89; N 4.53.

2-[(*Z*)-2-Hydroxy-2-(4-chlorophenyl)-1-ethenyl]-4*H*-3,1-benzoxazin-4-one (IIIe). Yield 96 (*a*), 100% (*b*), mp 205–206°C (2-propanol). IR spectrum, ν, cm^{-1}: 3170 br (OH_{bound}), 1757 (C^4=O), 1628 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.92 s (1H, CH), 7.36–8.15 group of signals (8H, $2C_6H_4$), 14.24 s (1H, OH). Found, %: C 64.10; H 3.37; Cl 11.85; N 4.65. $C_{16}H_{10}ClNO_3$. Calculated, %: C 64.12; H 3.36; Cl 11.83; N 4.67.

2-[(*Z*)-2-Hydroxy-2-(4-bromophenyl)-1-ethenyl]-4*H*-3,1-benzoxazin-4-one (IIIf). Yield 95 (*a*), 100% (*b*), mp 204–205°C (2-propanol). IR spectrum, ν, cm^{-1}: 3340 br (OH_{bound}), 1760 (C^4=O), 1625 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.91 s (1H, CH), 7.35–8.14 group of signals (8H, $2C_6H_4$), 14.23 s (1H, OH). Found, %: C 55.83; H 2.95; Br 23.25; N 4.05. $C_{16}H_{10}BrNO_3$. Calculated, %: C 55.84; H 2.93; Br 23.22; N 4.07.

The study was carried out under a financial support of the Russian Foundation for Basic Research (grants nos. 04-03-33024, 04-03-96033).

REFERENCES

1. Aliev, Z.G., Krasnykh, O.P., Maslivets, A.N., and Atovmyan, L.O., *Izv. Akad. Nauk, Ser. Khim.,* 2000, p. 2080.
2. Procop, P., Richter, R., and Beyer, L., *Z. Naturforsch. B*, 1999, vol. 54, p. 849.
3. Insuasty, B., Fernandez, F., Quiroga, J., Moreno, R., Martinez, R., Angeles, E., Gavino, R., Regina, H, de Almeida, S., *J. Heterocycl. Chem.,* 1998, vol. 35, p. 977.
4. Duke, N.E-C. and Codding, P.W., *Acta Cryst*., B49, p. 719.
5. Katritzky, A.R., Fan, W-Q., Koziol, A.E., and Palenik, G., *J. Heterocycl. Chem*., 1989, vol. 26, p. 821.
6. Andreichikov, Yu.S., Gein, V.L., Kozlov, A.P., and Vinokurova, O.V., *Zh. Org. Khim*., 1988, vol. 24, p. 210.
7. Andreichikov, Yu.S., Vinokurova, O.V., and Gein, V.L., *Zh. Org. Khim*., 1989, vol. 25, p. 2431.
8. Staskun, B. and Israelstam, S.S., *J. Org. Chem.,* 1961, vol. 26, p. 3191.
9. Vostrov, E.S. and Maslivets, A.N., Abstracts of Papers, *2nd Int. Conf*., Moscow: IBS PRESS, 2003, vol. 2, p. 270.
10. Maslivets, A.N., Lisovenko, N.Yu., Golovnina, O.V., Vostrov, E.S., and Tarasova, O.P., *Khim. Geterotsikl. Soedin.,* 2000, vol. 4, p. 556.
11. Altomare, A., Cascarano, G., Giacovazzo, C., and Gualardi, A., *J. Appl. Cryst.,* 1993, vol. 26, p. 343.
12. Sheldrick, G.M., *Shelx97. Programs for Crystal Structure Analysis,* University of Gottingen, Germany, 1998.